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Percutaneous freezing of sensory nerves prior to total knee arthroplasty

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ABSTRACT

Background: Total knee arthroplasty (TKA) is a common procedure resulting in significant post-operative pain. Percutaneous cryoneurolysis targeting the infrapatellar branch of the saphenous nerve and anterior femoral cutaneous nerve could relieve post-operative knee pain by temporarily blocking sensory nerve conduction.
Methods: A retrospective chart review of 100 patients who underwent TKA was conducted to assess the value of adding perioperative cryoneurolysis to a multimodal pain management program. The treatment group consisted of the first 50 patients consecutively treated after the practice introduced perioperative (five days prior to surgery) cryoneurolysis as part of its standard pain management protocol. The control group consisted of the 50 patients treated before cryoneurolysis was introduced. Outcomes included hospital length of stay (LOS), post-operative opioid requirements, and patient-reported outcomes of pain and function.
Results: A significantly lower proportion of patients in the treatment group had a LOS of ≥2 days compared with the control group (6% vs. 67%, $p < 0.0001$) and required 45% less opioids during the first 12 weeks after surgery. The treatment group reported a statistically significant reduction in symptoms at the six- and 12-week follow-up compared with the control group and within-group significant reductions in pain intensity and pain interference at two- and six-week follow-up, respectively.
Conclusions: Perioperative cryoneurolysis in combination with multimodal pain management may significantly improve outcomes in patients undergoing TKA. Promising results from this preliminary retrospective study warrant further investigation of this novel treatment in prospective, randomized trials.
Level of evidence: III

1. Introduction

Total knee arthroplasty (TKA) is a very common surgery for advanced osteoarthritis of the knee that is unresponsive to conservative treatments. There are approximately 600,000 knee replacements performed each year, and this number is expected to increase in future years [1]. Although knee replacements usually are very successful in the long term, patients often experience a significant amount of pain during the immediate post-operative period, which can be a major hindrance to effective rehabilitation and restoration of function following surgery.

Perioperative pain control has been the focus of considerable attention in recent years. Traditionally, narcotic pain medications have been used to control pain; however, their well-known side effects, such as nausea, emesis, ileus, and dependence, can slow down recovery [2]. Recently, multimodal pain management has been promoted to improve perioperative pain control while minimizing the risk of adverse events in the American Society of Anesthesiologists practice guidelines for acute pain management [3]. Multimodal pain management protocols implemented after total hip and knee arthroplasty (THA and TKA) have been shown to result in better pain control and patient satisfaction, lower overall narcotic consumption, shorter hospital stays, improved function, and fewer complications [4].

The use of cold as an analgesic dates back to the days of Hippocrates and the ancient Egyptians [5]. Recent work has shown the effect of cryoneurolysis on peripheral sensory nerve function. Barnard demonstrated that cryoneurolysis applied to the terminal branches of the trigeminal nerve in rats causes degeneration distal to the site of freezing without disruption of the anatomical architecture followed by structural regeneration of the nerve at about six weeks of post-injury and recovery of normal sensation in two to four months [6]. Histological studies have shown that treatment of nerves with temperatures from −20° to −60 °C results in Wallerian degeneration [6], which occurs distal to the site of injury and involves loss of the relative continuity of the axon and its covering of myelin, but preservation of the surrounding endoneurial, perineurial, and epineurial structure, which allows for normal axonal regeneration and remyelination [6]. Functional recovery of

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the sensory axon will normally occur between several weeks and months after cryoneurolysis depending on the distance of the axon injury site to the target site and rate of axon regrowth [6].

In a preclinical study, Hsu and Stevenson observed significant axonal regeneration and remyelination with concurrent elimination of macrophage infiltration and via histological examination of nerves eight weeks following cryoneurolysis and complete axonal regeneration by 16 weeks post-treatment [7]. Consistent with these findings, cryoneurolysis of peripheral sensory nerves has been shown to be efficacious in attenuating pain symptoms in patients with clinical conditions including trigeminal neuralgia, neuroma, and post-thoracotomy pain [5,8–12], with pain relief ranging from a couple of months to a few years [10,13].

Neuropathic knee pain is an important source of post-operative pain [13]. Percutaneous cryoneurolysis directed at sensory nerves that innervate the knee is a new option for reducing TKA post-operative pain [13]. Cryoneurolysis treatment of knee pain targets the infrapatellar branch of the saphenous nerve (ISN) and anterior femoral cutaneous nerve (AFCN), which lie in a predictable and superficial location as they approach the knee. The ISN and AFCN provide sensory innervation around the anterior knee with no motor involvement. After extensive use by the senior author in treatment of knee osteoarthritis pain, he began using this new treatment to improve post-operative outcomes following TKA. This study was conducted to evaluate whether perioperative cryoneurolysis, in combination with a standard multimodal pain regimen, would shorten hospital stays, decrease narcotic medication use, and improve patient-reported outcomes.

2. Materials & methods

2.1. Patient selection and methods

This was a retrospective chart review of 100 patients who underwent TKA by a single surgeon at a university-based orthopedic practice from 2011 to 2014. The treatment group (cryoneurolysis plus multimodal pain management) included the first 50 patients who were treated with cryoneurolysis after March 31, 2014, when the practice began administering perioperative cryoneurolysis to all TKA patients as part of its standard perioperative pain management protocol. This was the only appreciable change in practice and all other aspects of the treatment protocol (e.g., intraoperative and post-operative pain protocol, surgical technique, implant selection) remained the same. The control group consisted of the first 50 patients who were treated with multimodal pain management alone, preceding the introduction of the cryoneurolysis plus multimodal pain management regimen, who had completed the Western Ontario and McMaster Universities Arthritis Index (WOMAC).

Among the 100 patients included in the study, 70 were females and 30 males. As shown in Table 1, the treatment and control groups were similar in terms of gender ($p = 0.66$), age ($p = 0.24$), and body mass index (BMI) ($p = 0.26$). There were no overall significant differences between groups on baseline patient-reported outcome measures (Wilks' F-test, $p = 0.73$, Table 2). The treatment group received cryoneurolysis of the AFCN and ISN five days prior to surgery in addition to the standard preoperative multimodal pain management program.

Table 1
Patient demographics.

	Control (N = 50)	Treatment (N = 50)	p value
Gender			0.66
Male, N (%)	14 (46.7)	16 (53.3)	
Female, N (%)	36 (51.4)	34 (48.6)	
Age (years), mean (SD)	66.4 (9.4)	68.5 (8.2)	0.24
Body mass index (kg/m^2), mean (SD)	30.9 (5.7)	32.1 (5.3)	0.26

Table 2
Baseline clinical characteristics.

Variable		Control	Treatment	p value
KOOS				
Activities of daily living	N	46	49	0.82
	Mean (SD)	41.07 (21.97)	40.14 (17.51)	
Pain	N	46	49	0.57
	Mean (SD)	36.04 (20.82)	38.18 (15.38)	
Quality of life	N	44	49	0.29
	Mean (SD)	22.16 (23.42)	17.86 (15.34)	
Sports and rec	N	31	37	0.70
	Mean (SD)	25.58 (31.54)	22.68 (29.62)	
Symptoms	N	46	49	0.53
	Mean (SD)	44.11 (19.32)	41.80 (16.74)	
Oxford Knee Score	N	46	46	0.97
	Mean (SD)	18.72 (10.30)	18.78 (8.45)	
PROMIS				
Anxiety	N	18	41	0.32
	Mean (SD)	58.78 (12.88)	55.45 (11.11)	
Depression	N	19	45	0.5
	Mean (SD)	51.03 (11.17)	49.14 (9.71)	
Fatigue	N	18	44	0.85
	Mean (SD)	53.23 (8.74)	52.73 (10.07)	
Pain interference	N	18	46	0.69
	Mean (SD)	65.27 (8.23)	66.13 (7.60)	
Pain intensity	N	18	46	0.93
	Mean (SD)	6.83 (2.90)	6.89 (2.16)	
Sleep disturbances	N	17	41	0.16
	Mean (SD)	54.45 (9.41)	51.14 (7.48)	
Social satisfaction	N	18	43	0.86
	Mean (SD)	39.83 (10.63)	40.42 (12.10)	
Physical function	N	19	43	0.12
	Mean (SD)	35.49 (6.49)	33.05 (5.17)	
SF-12 mental component	N	30	41	0.01
	Mean (SD)	42.77 (12.28)	50.00 (10.43)	
SF-12 physical component	N	30	41	0.22
	Mean (SD)	30.76 (7.12)	28.77 (6.41)	
WOMAC				
Function	N	50	49	0.99
	Mean (SD)	41.92 (22.10)	41.90 (17.00)	
Pain	N	50	49	0.74
	Mean (SD)	41.20 (22.69)	42.55 (17.74)	
Stiffness	N	50	49	0.39
	Mean (SD)	40.82 (26.19)	36.94 (17.03)	

KOOS = Knee Injury and Osteoarthritis Outcome Score; PROMIS = Patient-reported Outcomes Measurement Information System; SD = standard deviation; SF-12 = **12**-item Short Form Health Survey; WOMAC = Western Ontario and McMaster Universities Arthritis Index.

Cryoneurolysis was administered using a novel handheld device, iovera (Myoscience, Fremont California, Figure 1), which was FDA approved (K100447 and K133453) in 2012 to produce "lesions in peripheral nervous tissue by the application of cold to the selected site for the blocking of pain." This device converts liquid nitrous oxide into a gas, creating temperatures of −125 °F along three hollow closed tip short needles (27 gauge, 6 mm long), introduced percutaneously at a target site, to produce a five millimeter cold zone (ice ball) under the skin. Ice ball contact with the target nerve causes Wallerian degeneration, creating axonotmesis while maintaining the original surrounding anatomy (maintaining the scaffold) to allow predictable regrowth of the axon along the original epineurium and endoneurium. The maximum cold temperature produced by the device has no known permanent risks because the original structural scaffold of the nerve is preserved. There are limited transient side effects, such as bruising and tenderness where the needles are inserted.

Treatments were done in the office five days before planned TKA. The AFCN and ISN and their branches were targeted along two treatment lines. The AFCN was targeted approximately 70 mm above the superior pole of the patella along a horizontal line the width of the patella. The AFCN lies within the fascia overlying the quadriceps tendon deep to the subcutaneous fat (Figure 2). The ISN was targeted approximately 50 mm medial to the patella tendon (Figure 3) along a longitudinal line from the inferior pole of the patella and tibial tubercle. The ISN